Attorney's Docket No.: 14875-057001 / C2-906DP1PCT-US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Jun-ichi Nezu et al.
Serial No. : 09/521,195
Filed : March 7, 2000

Art Unit : 1646
Examiner : P. Mertz
Confirmation No.: 9418
Notice of Allowance Date: November 20, 2004

Title : TRANSPORTER POLYPEPTIDE AND METHOD OF PRODUCING SAME

Attention: Official Draftsman
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL OF FORMAL DRAWINGS

In response to the Notice Regarding Drawings mailed March 10, 2004, please substitute the enclosed thirteen (13) sheets of formal drawings for the corresponding drawings presently in the application.

Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: May 7, 2004

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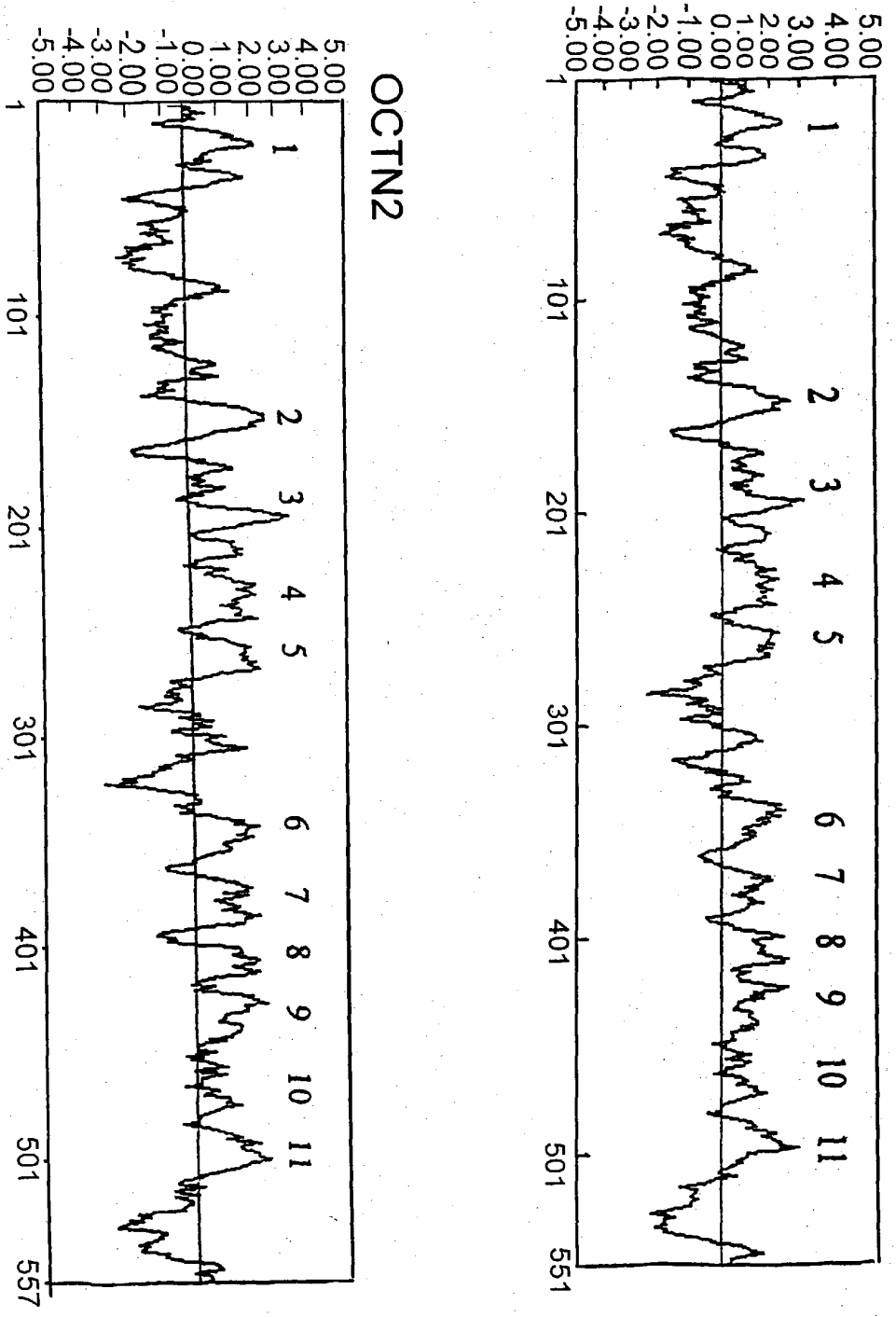

OCTN1
5.00
4.00
3.00
2.00
1.00
0.00
-1.00
-2.00
-3.00
-4.00
-5.00
1
101
201
301
401
501
551
1 2 3 4 5 6 7 8 9 10 11
OCTN2
5.00
4.00
3.00
2.00
1.00
0.00
-1.00
-2.00
-3.00
-4.00
-5.00
1
101
201
301
401
501
557
1 2 3 4 5 6 7 8 9 10 11

FIG. 1

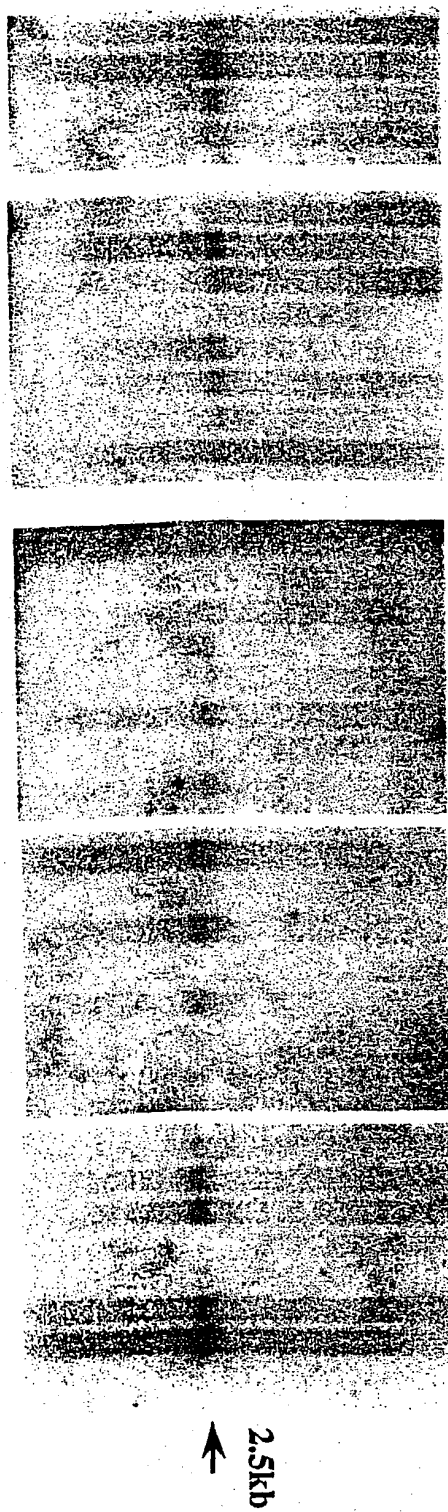

KIDNEY
LIVER
LUNG
BRAIN
PANCREAS
KIDNEY
SKELETAL MUSCLE
LIVER
LUNG
PLACENTA
BRAIN
HEART
PERIPHERAL BLOOD LEUKOCYTE
COLON
SMALL INTESTINE
UTERUS
TESTIS
PROSTATE
THYMUS
SPLEEN
BONE MARROW
ADRENAL GLAND
TRACHEA
LYMPH NODE
SPINAL CORD
THYROID GLAND
STOMACH
MELANOMA G361
LUNG CANCER A549
LARGE INTESTINE ADENOCARCINOMA SW480
BURKITT'S LYMPHOMA RAJI
LYMPHOBLASTIC LEUKEMIA MOLT-4
CHRONIC MYELOCYTIC LEUKEMIA K-562
CERVICAL CARCINOMA HeLa S3
PROMYELOCYTIC LEUKEMIA HL-60
2.5kb
HUMAN FETAL TISSUES
HUMAN ADULT TISSUES
CELL LINES DERIVED FROM HUMAN CANCER

FIG. 2

Appln No.: 09/521,195
Applicant(s): Jun-ichi Nezu et al.
TRANSPORTER POLYPEPTIDE AND METHOD OF PRODUCING SAME

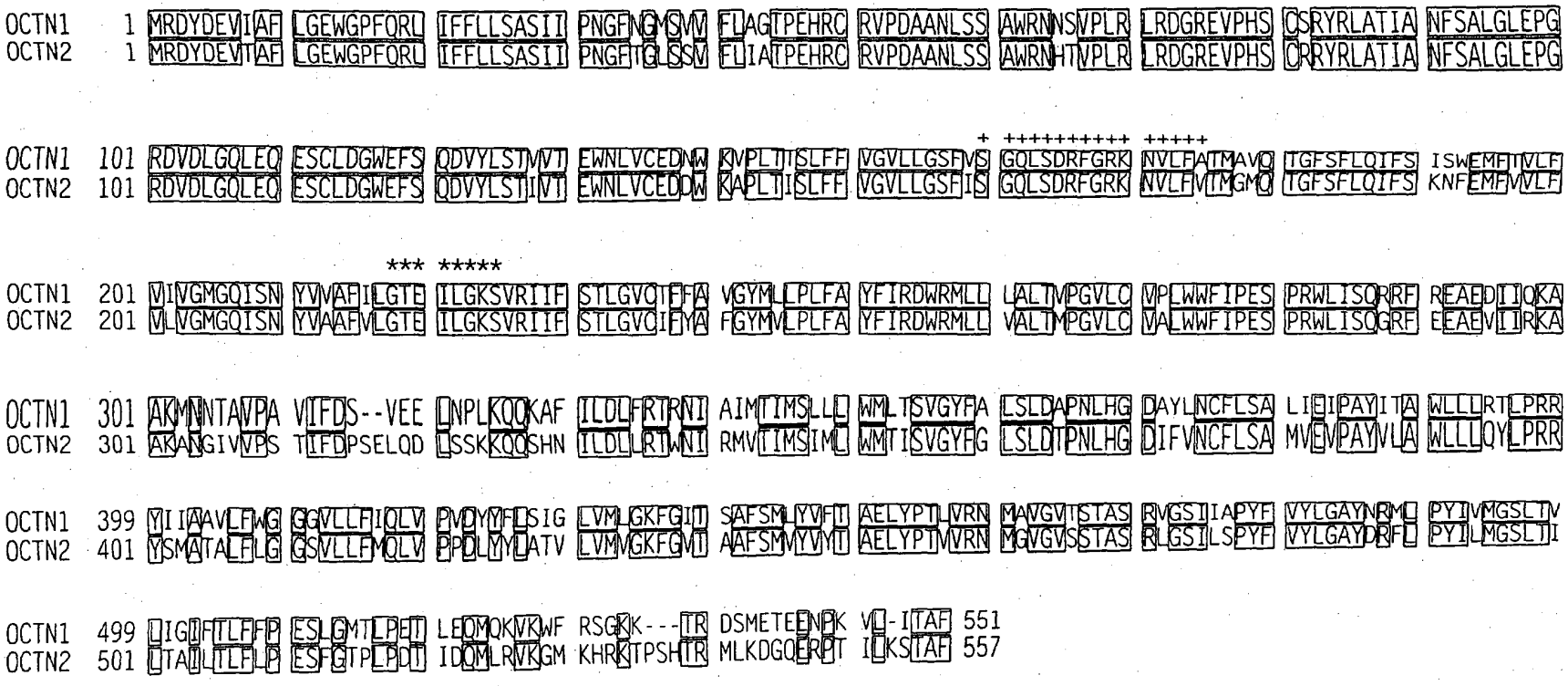
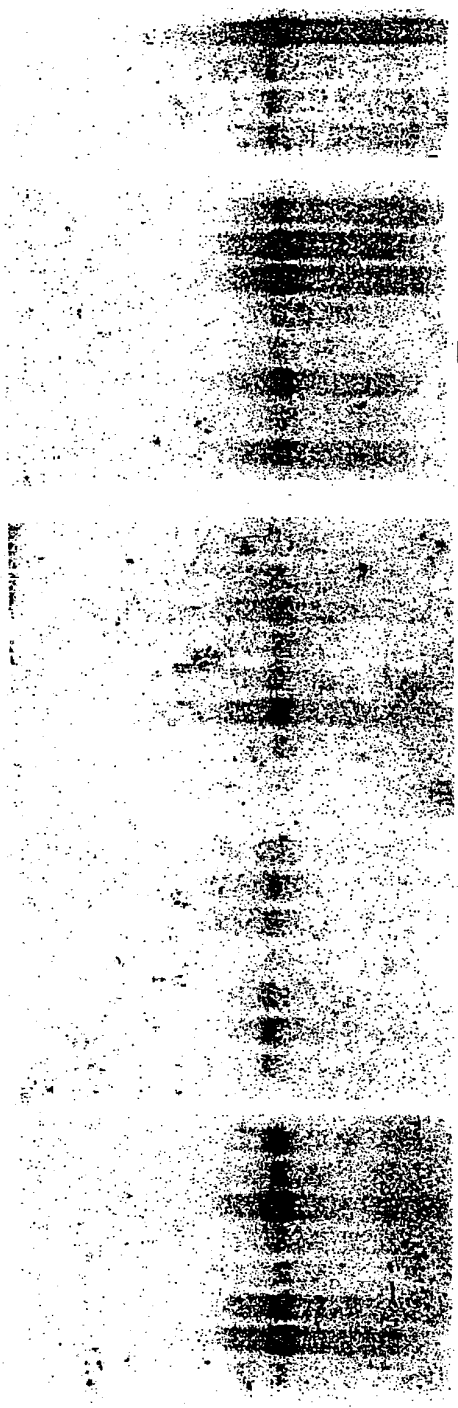


FIG. 3


KIDNEY
LIVER
LUNG
BRAIN
PANCREAS
KIDNEY
SKELETAL MUSCLE
LIVER
LUNG
PLACENTA
BRAIN
HEART
PERIPHERAL BLOOD LEUKOCYTE
COLON
SMALL INTESTINE
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BURKITT'S LYMPHOMA RAJI
LYMPHOBLASTIC LEUKEMIA MOLT-4
CHRONIC MYELOCYTIC LEUKEMIA K-562
CERVICAL CARCINOMA HeLa S3
PROMYELOCYTIC LEUKEMIA HL-60
3.0 kb
HUMAN FETAL TISSUES
HUMAN ADULT TISSUES
CELL LINES DERIVED FROM HUMAN CANCER

FIG. 4

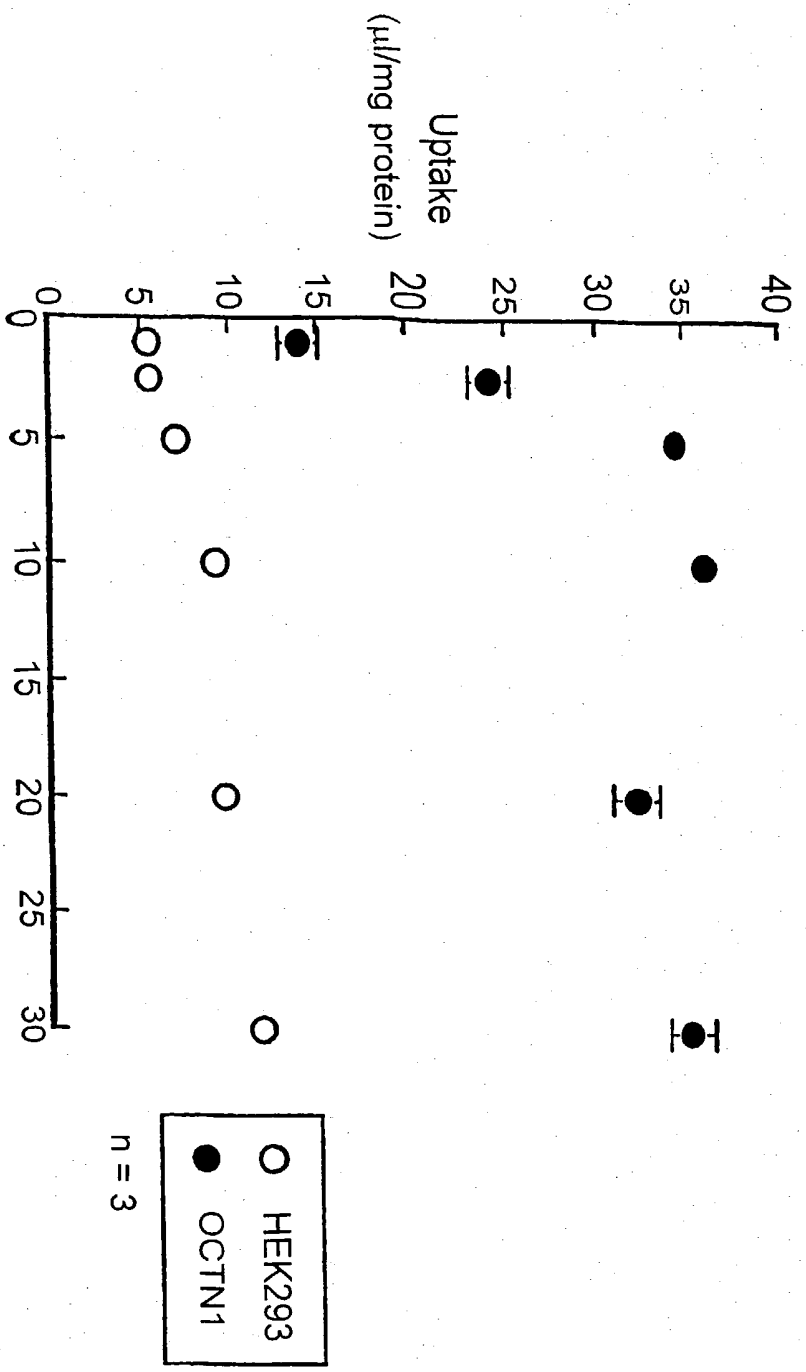

Uptake
(μl/mg protein)
0
5
10
15
20
25
30
35
40
Time (min)
0
5
10
15
20
25
30
HEK293
OCTN1
n = 3

FIG. 5

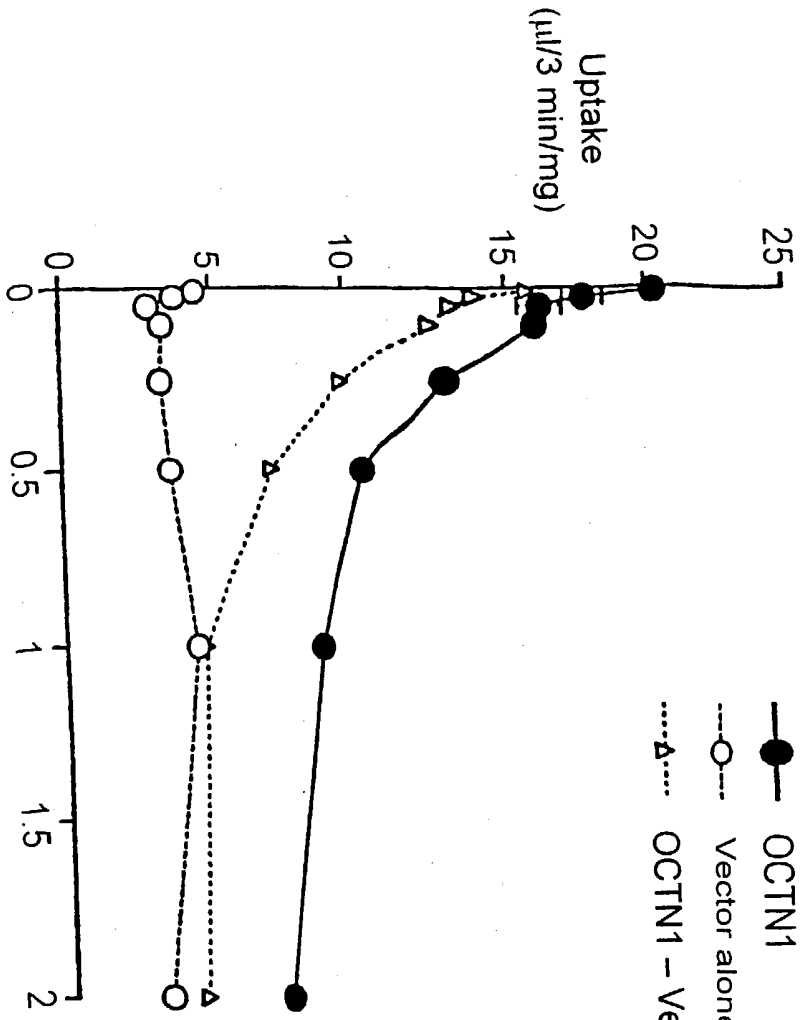

Uptake
(μl/3 min/mg)
0
5
10
15
20
25
0
0.5
1
1.5
2
Concentration (mM)
OCTN1
Vector alone
OCTN1 – Vector alone

FIG. 6

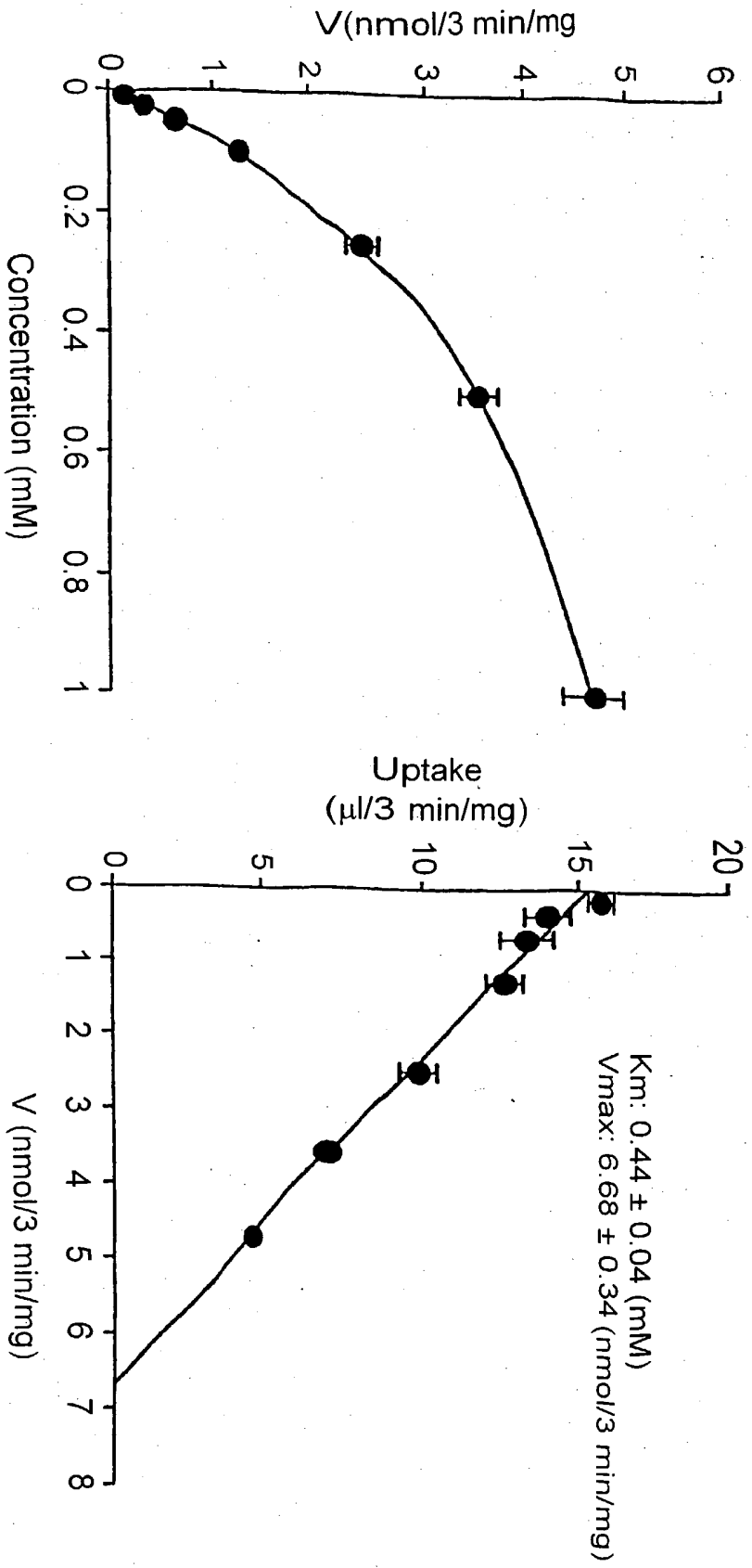

V(nmol/3 min/mg
0
1
2
3
4
5
6
0
0.2
0.4
0.6
0.8
1
Concentration (mM)
Uptake
(μl/3 min/mg)
0
5
10
15
20
0
1
2
3
4
5
6
7
8
V (nmol/3 min/mg)
Km: 0.44 ± 0.04 (mM)
Vmax: 6.68 ± 0.34 (nmol/3 min/mg)

FIG. 7

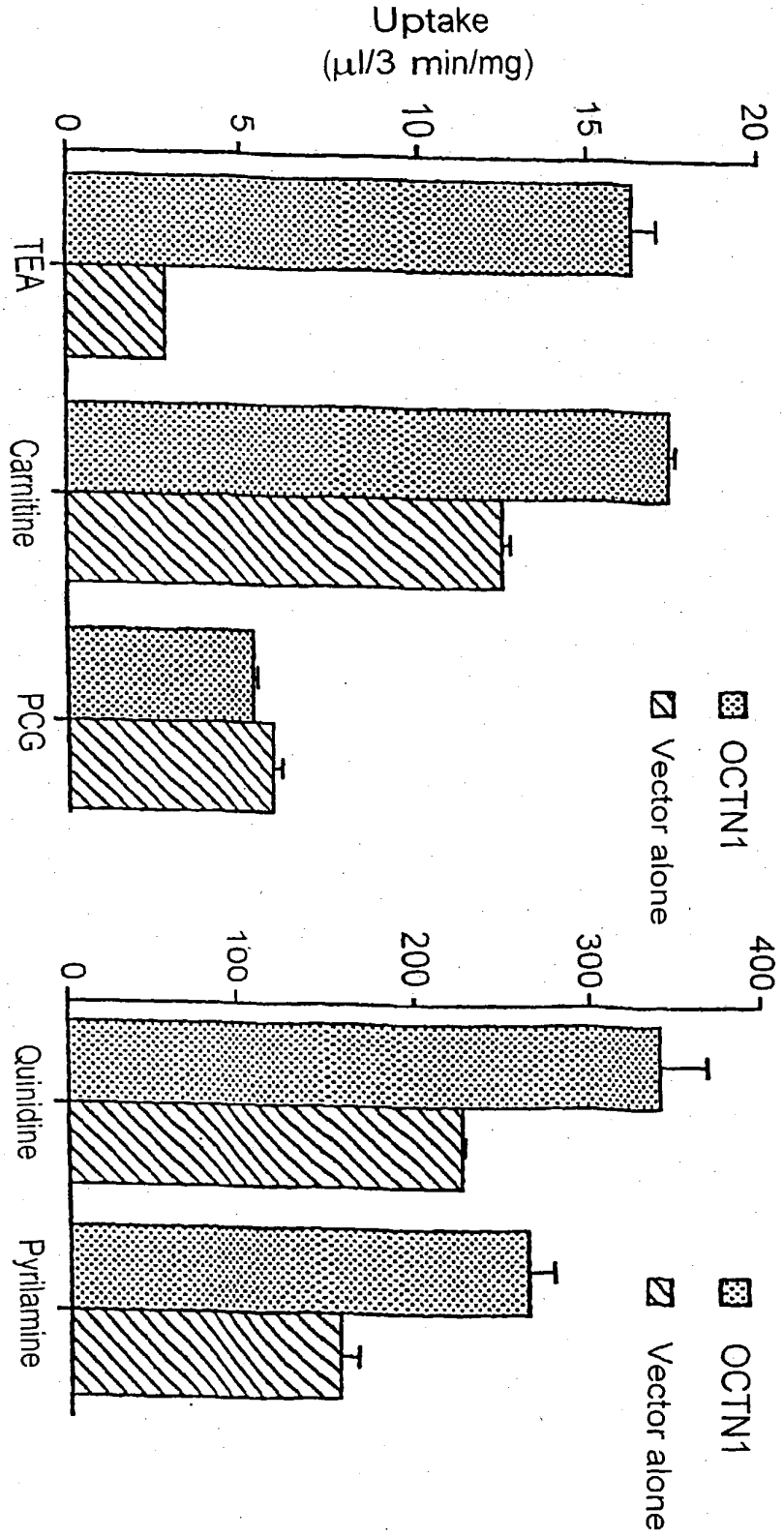

Uptake
(μl/3 min/mg)
0
5
10
15
20
TEA
Carnitine
PCG
OCTN1
Vector alone
0
100
200
300
400
Quinidine
Pyrilamine
OCTN1
Vector alone

FIG. 8

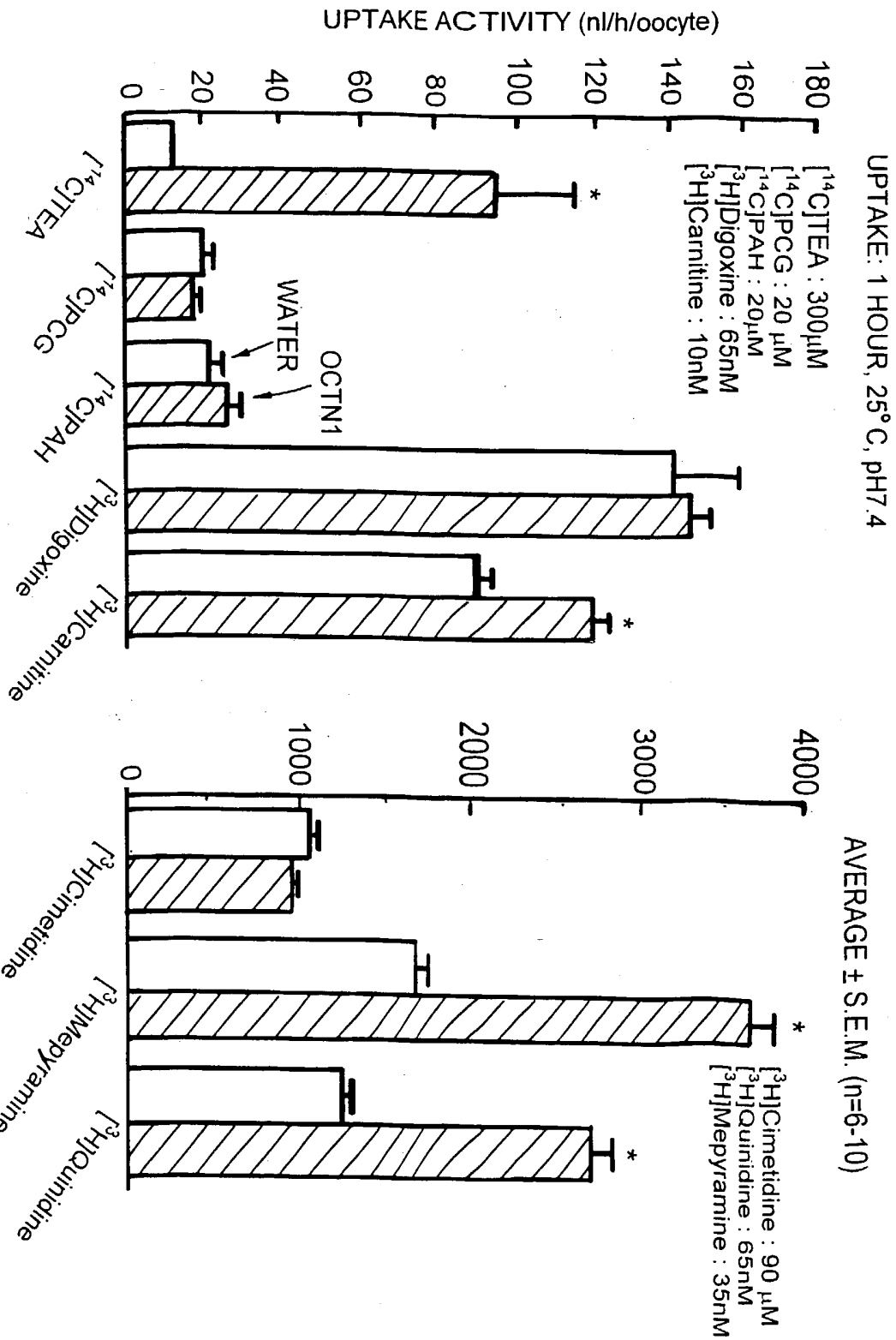

UPTAKE ACTIVITY (nl/h/oocyte)
0
20
40
60
80
100
120
140
160
180
[14C]TEA
[14C]PCG
[14C]PAH
[3H]Digoxine
[3H]Carnitine
WATER
OCTN1
*
*
UPTAKE: 1 HOUR, 25° C, pH7.4
[14C]TEA : 300μM
[14C]PCG : 20 μM
[14C]PAH : 20μM
[3H]Digoxine : 65nM
[3H]Carnitine : 10nM
0
1000
2000
3000
4000
[3H]Cimetidine
[3H]Mepyramine
[3H]Quinidine
*
*
AVERAGE ± S.E.M. (n=6-10)
[3H]Cimetidine : 90 μM
[3H]Quinidine : 65nM
[3H]Mepyramine : 35nM

FIG. 9

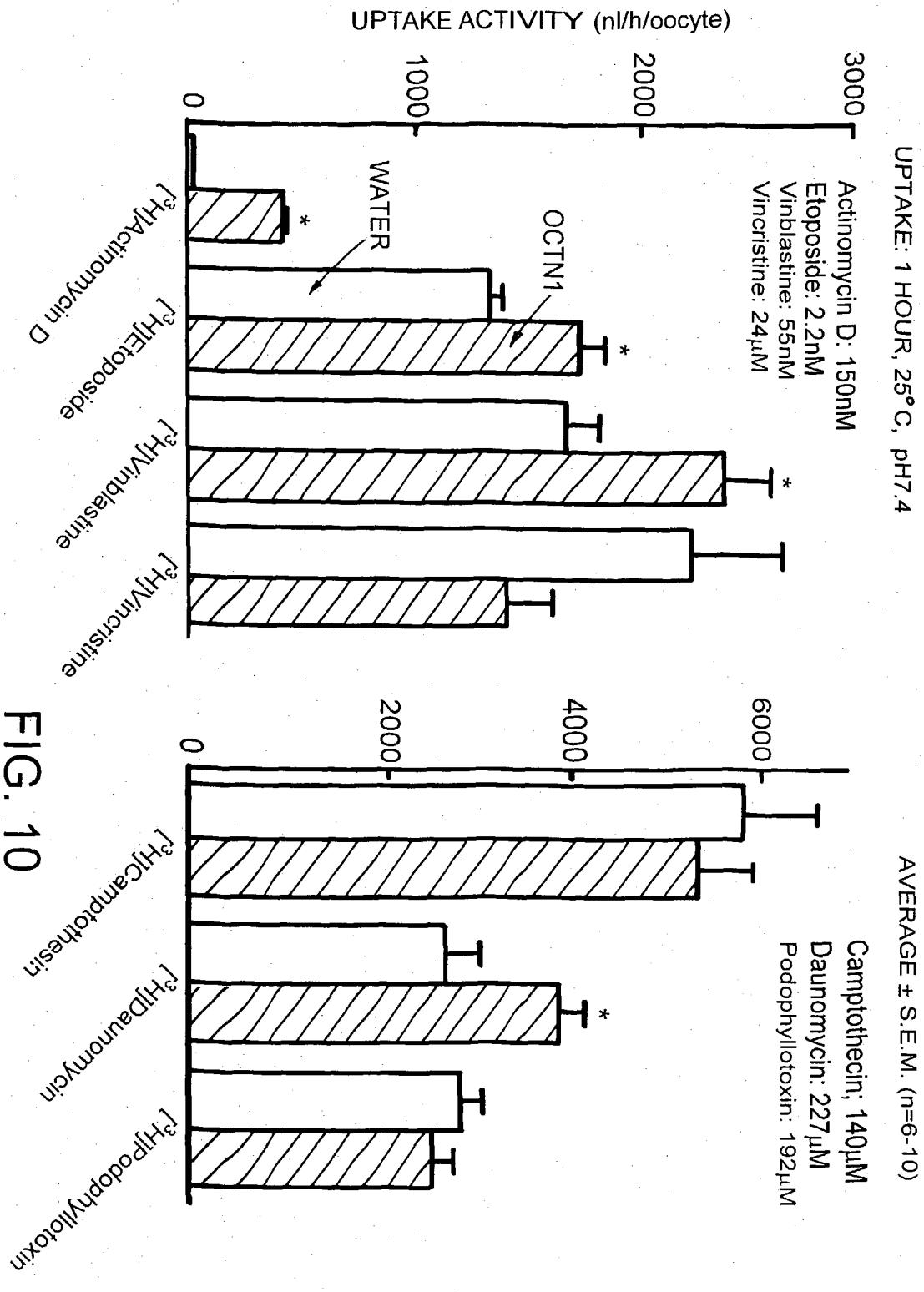
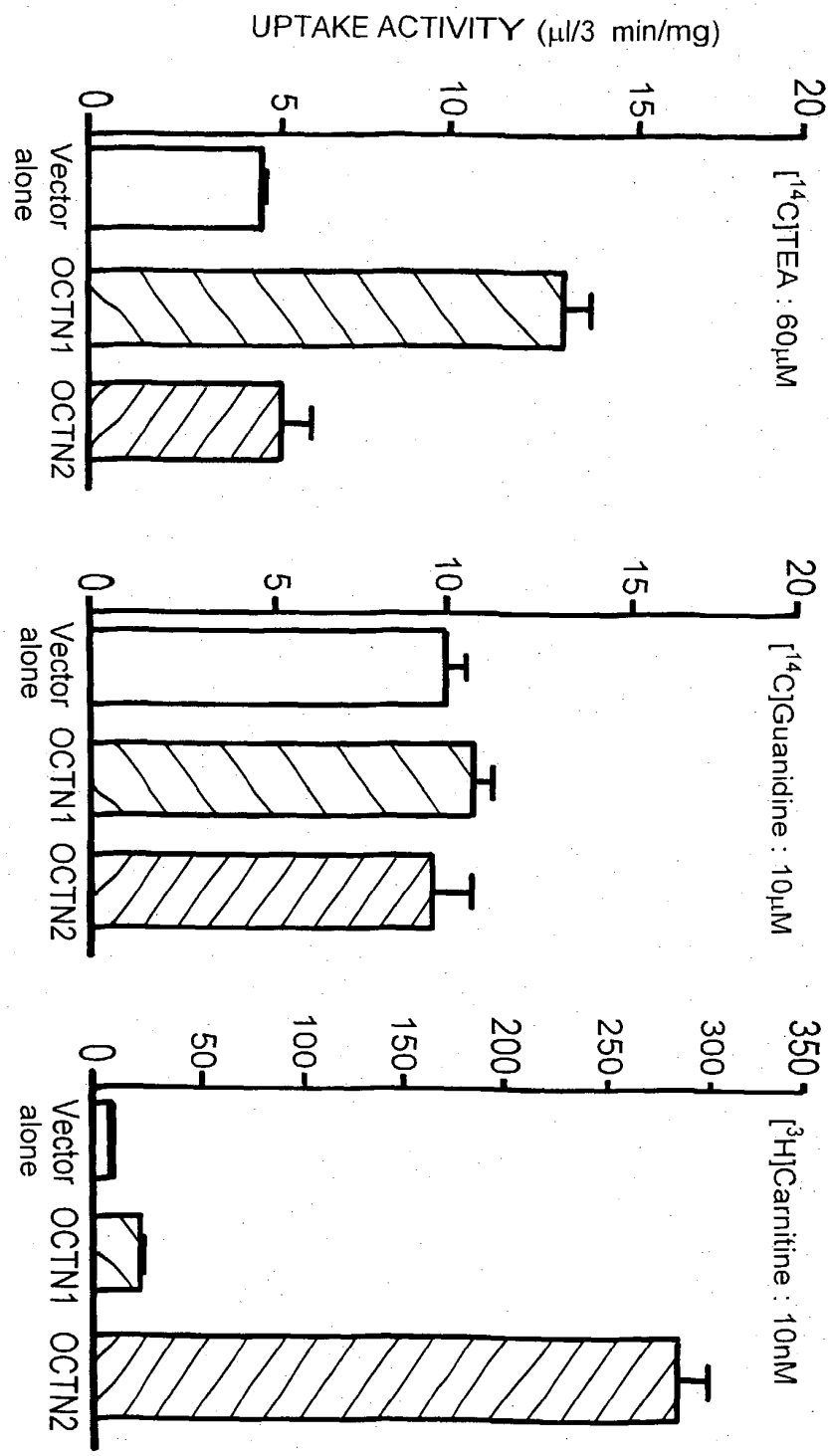

UPTAKE ACTIVITY (nl/h/oocyte)
0
1000
2000
3000
WATER
OCTN1
*
[3H]Actinomycin D
[3H]Etoposide
[3H]Vinblastine
[3H]Vincristine
Actinomycin D: 150nM
Etoposide: 2.2nM
Vinblastine: 55nM
Vincristine: 24μM
UPTAKE: 1 HOUR, 25°C, pH7.4
0
2000
4000
6000
[3H]Camptothecin
[3H]Daunomycin
[3H]Podophyllotoxin
Camptothecin; 140μM
Daunomycin: 227μM
Podophyllotoxin: 192μM
AVERAGE ± S.E.M. (n=6-10)

FIG. 10



Uptake: 3 min, 37°C, pH7.4

FIG. 11

Average ± S.E.M. (n = 3)

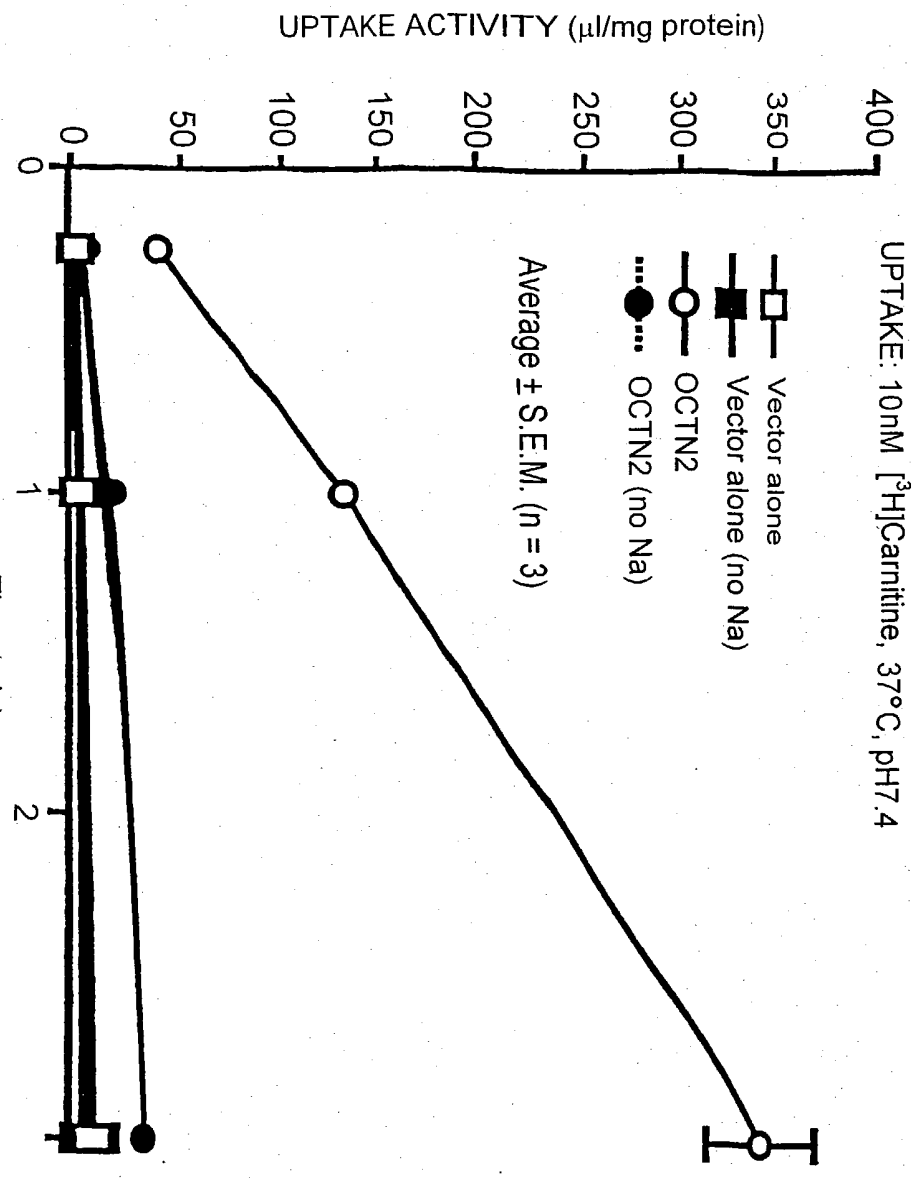

UPTAKE ACTIVITY (μl/mg protein)
0
50
100
150
200
250
300
350
400
0
1
2
Time (min)
UPTAKE: 10nM [3H]Carnitine, 37°C, pH7.4
Vector alone
Vector alone (no Na)
OCTN2
OCTN2 (no Na)
Average ± S.E.M. (n = 3)

FIG. 12

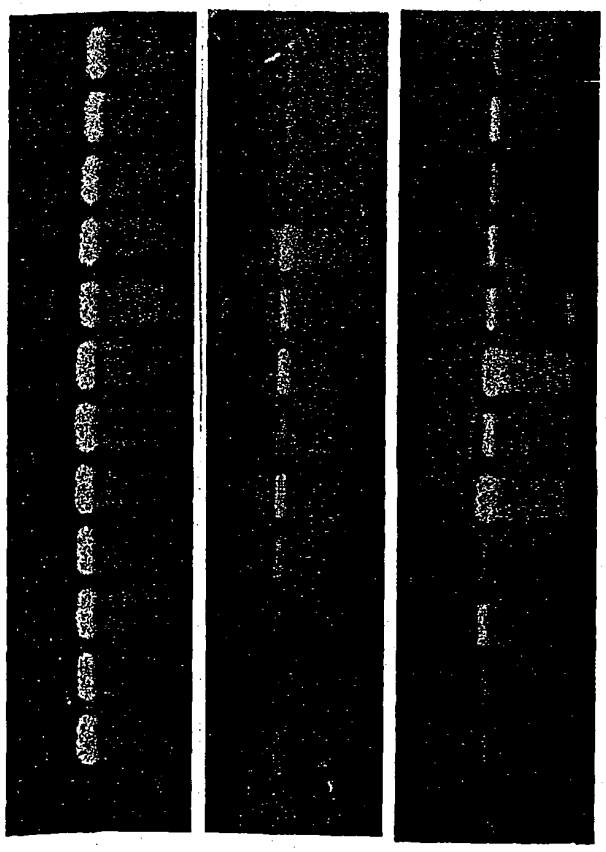

mouse OCTN 1
mouse OCTN 2
G3PDH
17 day
15 day
11 day
7 day
Testis
Kidney
Sk. Muscle
Liver
Lung
Spleen
Brain
Heart
No DNA
Embryo
Adult Tissues

FIG. 13